JACC Vol. 17, No. 1
January 1991:189–92

In-Hospital Mortality After Balloon Aortic Valvuloplasty: Frequency And Associated Factors

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Percutaneous balloon aortic valvuloplasty has been accompanied by significant early periprocedural morbidity and mortality. Identification of factors associated with increased mortality might allow for improved selection of patients. The Mansfield Scientific Balloon Aortic Valvuloplasty Registry was analyzed to identify the frequency of in-hospital death and the factors associated with it. Of 492 patients undergoing the procedure, 37 (7.5%) died during the hospital stay in which valvuloplasty was performed. Twenty-four of these patients died within the first 24 h and the remainder died within 7 days after the procedure.

There were significant differences in baseline clinical and hemodynamic characteristics as well as procedural and postprocedural variables between patients dying and those surviving the in-hospital period. Multivariate analysis identified four factors associated with increased mortality: 1) the occurrence of a procedure-related complication, 2) a lower initial left ventricular systolic pressure, 3) a smaller final aortic valve area, and 4) a lower baseline cardiac output.

Thus, baseline hemodynamic, procedural and postprocedural variables and complications can be identified that are associated with increased mortality.

(J Am Coll Cardiol 1991;17:189–92)

Balloon aortic valvuloplasty has been used to treat severe aortic stenosis in patients who are at high risk for aortic valve replacement (1–5). This high risk group includes very elderly patients, those with depressed left ventricular function and those with associated medical conditions that make conventional treatment with aortic valve replacement less optimal. Valvuloplasty in these patients results in moderate improvement in aortic valve hemodynamics (2,3,6,7). There is, however, a substantial incidence of early complications, including vascular entry problems, ventricular arrhythmias, left ventricular perforation and death (2–5,8). Identification of factors associated with increased early mortality would improve patient selection and perhaps outcome. This study analyzed data from the Mansfield Scientific Balloon Aortic Valvuloplasty Registry to assess early mortality and identify clinical, hemodynamic and procedural factors associated with early death.

Methods

Selection of patients. The Mansfield Scientific Balloon Aortic Valvuloplasty Registry is an industry-sponsored study performed under the auspices of a Food and Drug Administration-approved investigational device exemption. As part of an early evaluation of the safety and efficacy of percutaneous balloon aortic valvuloplasty, 27 centers prospectively entered baseline clinical and hemodynamic data, procedural data and follow-up data on 492 consecutive patients undergoing this procedure for the treatment of severe aortic stenosis at these centers from December 1, 1986 to October 30, 1987. These patients form the basis of this report.

The indications for valvuloplasty at each center varied somewhat, but by recommendation they included symptomatic aortic stenosis with no or only mild aortic regurgitation in patients who were not thought to be ideal candidates for conventional treatment with aortic valve replacement. The clinical reasons for proceeding with balloon aortic valvuloplasty instead of aortic valve replacement were determined at each center, but they included advanced age, significant left ventricular dysfunction, the presence of associated cardiovascular or noncardiac diseases that would adversely affect surgical treatment or outcome and physician or patient preference.

Analysis of data (Table 1). In-hospital mortality was assessed. Factors associated with increased mortality were identified with univariate analysis. Discrete variables were tested by chi-square analysis and continuous variables were assessed with a two-tailed *t* test. Factors associated with increased mortality by univariate analysis were further evaluated with multivariate discriminant analysis. Because complications of the procedure were found to be an important predictor of in-hospital death, both univariate and multivariate analyses were performed to assess factors associated with complications (Table 1).

Valvuloplasty was performed in all patients in a manner similar to that described by Cribier et al. (1,2). Success was

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0735-1097/91/$3.50

JACC Vol. 17, No. 1
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Table 1. Variables Assessed in 492 Patients Undergoing Balloon Aortic Valvuloplasty

Clinical	Hemodynamic	Procedural
Age	Left ventricular systolic pressure	Maximal balloon size
Gender	Left ventricular diastolic pressure	One vs. two balloons
History of myocardial infarction	Aortic valve area	Complications
Symptoms	Mean aortic valve gradient	Embolic event
Dyspnea	Cardiac output*	Vascular injury
Angina		Cardiac arrest
Heart failure		Ventricular perforation
Syncope		Aortic regurgitation
Fatigue		Aortic valve replacement
NYHA functional class		Ventricular tachycardia
Coronary artery disease†		Ventricular fibrillation
None		Infarction
1 vessel		Hypotension
2 vessel		Heart failure
3 vessel		

*Measured by indicator dilution, thermodilution or Fick method. †Significant stenosis was defined as ≥50% stenosis of a major epicardial vessel. NYHA = New York Heart Association.

defined as an increase in valve area of ≥25% or a decrease in pressure gradient of ≥50% and no death or valve replacement within 7 days.

Results

Results of angioplasty. Of the 492 patients, 219 were men and 273 were women; their mean age ± SD was 78.7 ± 8.4 years. The procedure was successful in 428 cases (87%). The mean initial aortic valve area increased from 0.50 ± 0.18 to 0.82 ± 0.30 cm^2, and the average mean gradient decreased from 59.8 ± 23.0 to 29.5 ± 13.4 mm Hg (Table 2).

Of the 492 patients, 37 (7.5%) died during the hospital stay in which valvuloplasty was performed. Twenty-four patients (4.9%) died within the first 24 h after the procedure and the remainder died between 24 h and 7 days after the procedure.

Factors Associated With Mortality

Baseline clinical and hemodynamic factors (Table 2). There were significant differences in the baseline clinical and hemodynamic characteristics of the patients who died during hospitalization and those who survived the in-hospital period. Patients who died had a lower mean initial aortic valve area (0.40 ± 0.02 versus 0.51 ± 0.01 cm^2, $p < 0.001$), lower baseline left ventricular systolic pressure (184 ± 7 versus 203 ± 2 mm Hg, $p < 0.01$) and lower baseline cardiac output (3.0 ± 0.2 versus 3.9 ± 0.1 liters/min, $p < 0.001$) than survivors. In addition, the incidence of coronary artery

Table 2. Comparison of Patients Who Had Procedure-Related and In-Hospital Death After Balloon Aortic Valvuloplasty and Patients Who Survived the Procedure, by Selected Baseline and Procedural Characteristics

Characteristic	Patient Group*		p Value
	Death (n = 37)	Survival (n = 455)	
Gender			NS
Male (%)	40	45	
Female (%)	60	55	
Age (yr) (mean ± SD)	80.1 ± 1.4	78.6 ± 0.4	NS
Cardiac output (liters/min)	3.0 ± 0.2 (36)	3.9 ± 0.1 (443)	0.001
Valve area (cm^2)	0.40 ± 0.02 (34)	0.51 ± 0.01 (454)	0.001
Valve gradient (mm Hg)	57.0 ± 4.1 (35)	60.0 ± 1.1	NS
Left ventricular systolic pressure (mm Hg)	184 ± 7 (36)	203 ± 2 (453)	0.01
Left ventricular diastolic pressure (mm Hg)	20 ± 2 (36)	19 ± 1 (452)	NS
NYHA class III or IV (%)	97 (31)	80 (411)	0.012
Final aortic valve area (cm^2)	0.68 ± 0.6 (27)	0.83 ± 0.01 (452)	0.02
Final valve gradient (mm Hg)	29.6 ± 4.0 (28)	29.5 ± 0.6 (454)	NS
Change in valve area (cm^2)	0.27 ± 0.06 (27)	0.32 ± 0.01 (452)	NS
Change in valve gradient (mm Hg)	24.0 ± 3.5 (28)	30.5 ± 0.8 (454)	NS
≥1 complication (%)	73	16	0.0001
Results of coronary arteriography (no. of patients)†			
Normal	4	172	
Mild stenosis	7	72	0.05
≥50% stenosis	16	174	
1 vessel disease	5	70	
2 vessel disease	2	45	NS
3 vessel disease	7	56	
Prior myocardial infarction (%)	13.5	10.1	NS

*n is given in parentheses for cases in which data were missing. †Because of missing data in some cases, not all patients in a group are accounted for. NYHA = New York Heart Association.

Table 3. Multivariate Analysis in 492 Patients Undergoing Balloon Aortic Valvuloplasty

Variables subjected to multivariate analysis
Prevalvuloplasty aortic valve area
Left ventricular peak systolic pressure
Cardiac output
Coronary artery disease
Number of inflations performed
Final aortic valve area
Change in aortic valve gradient
Incidence and number of procedure-related complications
Discriminant analysis of variables related to in-hospital death
Procedure-related complications
Lower initial left ventricular systolic pressure
Lower final aortic valve area
Lower baseline cardiac output

Table 4. Multivariate Analysis of Complications in 492 Patients Undergoing Balloon Aortic Valvuloplasty

Variables included in analysis
Gender
Age
Presence of coronary artery disease
Weight
Prevalvuloplasty functional class (New York Heart Association)
Use of double balloon technique
First 250 patients (early experience)
Number of balloons used
Variables selected for regression with increased likelihood of complications
Female gender
Presence of coronary artery disease
More severe baseline functional class (New York Heart Association)
Double balloon technique
Small number of patients (only 250)

disease in patients who died was significantly higher (85% versus 59%, $p < 0.05$).

Procedural factors (Tables 2 and 3). There were also significant differences in the procedural and postvalvuloplasty variables between survivors and those who died. The only hemodynamic variable that was significantly different was the mean aortic valve area after valvuloplasty, which was 0.68 ± 0.06 cm^2 in the patients who died and 0.83 ± 0.01 cm^2 in the survivors ($p < 0.02$). The frequency of complications also significantly affected outcome. Patients with one or more complications had a higher incidence of death ($p < 0.001$).

Variables identified with univariate analysis were then tested in a multivariate model (Table 3). The occurrence of procedural-related complications was the most important variable. The patients with an in-hospital complication had a 27% mortality rate, whereas those with no complications had a mortality rate of only 2.6%. The highest mortality rate was seen in association with myocardial perforation (56%), ventricular tachycardia or fibrillation (53%) and emergency valve replacement (33%). Other variables associated with increased mortality included the baseline variables of left ventricular function, specifically a lower baseline left ventricular systolic pressure and lower initial cardiac output. The final variable associated with increased mortality was final aortic valve area—the lower the final aortic valve area, the higher the incidence of death.

Factors Associated With Complications (Tables 1 and 4)

Because the occurrence of procedure-related complications was the most important variable associated with in-hospital death, an analysis was performed on factors (Table 1) associated with the development of complications. With univariate analysis, the only two significant variables were female gender ($p = 0.04$) and the presence of coronary artery disease ($p = 0.04$). Increasing severity of prevalvuloplasty functional class showed a trend toward significance ($p = 0.07$). The use of a double balloon technique was associated with a decreased incidence of vascular injury compared with a single balloon technique (5.0% versus 12.7%). This difference is probably related to the smaller caliber of balloons used in the double balloon technique. However, patients who had a double balloon procedure had a slightly increased incidence of acute aortic regurgitation.

Variables associated with the presence of a complication were assessed with multivariate analysis (Table 4). The association between these variables and the development of complications was highly significant ($p = 0.0016$); however, the model predicted complications accurately in only 58% of the patients. There was a decrease in the complication rate over time. In the first half of the study from December 1986 to July 1987, the overall complication rate was 25%, whereas in the last 231 patients from July 1987 to December 1987, the complication rate was 10% ($p < 0.05$). This decrease was primarily related to a decrease in vascular trauma.

Six patients underwent emergency aortic valve replacement after valvuloplasty. The procedure was performed for acute aortic regurgitation in four and left ventricular perforation in two; three of these six patients died within the first 30 days after operation.

Discussion

Indications for valvuloplasty. Although aortic valve replacement is the treatment of choice for patients with symptomatic aortic stenosis, there are subsets of patients in whom it is problematic. Although age is not itself a contraindication to valve replacement, the risks of operation are increased in elderly patients (9–12). In octogenarians, a perioperative 30 day mortality rate of 20% to 30% has been reported (11). In patients >70 years of age, the perioperative mortality rate ranges from 7% to 15%, depending on the degree of coronary artery disease and the need for other surgical procedures as well as on the baseline hemodynamic status (9,10,12). Magovern et al. (9) found a 25% operative

mortality rate in elderly patients with hemodynamic instability. There are other subsets of patients who, because they have associated medical conditions (for example, chronic obstructive lung disease or malignancy), either are not surgical candidates or are higher risk surgical candidates.

In these patient subsets, the use of percutaneous aortic balloon valvuloplasty has received considerable interest as an alternative treatment. However, subsequent to this initial enthusiasm, the risks and follow-up events in these patients have been the subject of concern (3–5,13). In-hospital mortality rates from 3.5% to 7.5% have been reported, and the follow-up incidence of restenosis is approximately 50% at 6 to 12 months. In the current series, the mortality rate was 7.5%. This series was composed of patients who underwent valvuloplasty from December 1, 1986 to October 30, 1987, and therefore the results represent an early experience with a new technique.

Factors associated with postvalvuloplasty mortality. In this series, the factors associated with an increased incidence of death included a lower left ventricular systolic blood pressure and a lower cardiac output at baseline; they thereby mirror the status of left ventricular function. In addition, patients who died during the in-hospital period had more severe aortic stenosis at baseline study. More important, a less successful procedure also was associated with poorer outcome; both a more severe residual stenosis and a smaller final aortic valve area were associated with increased mortality. The most powerful factor associated with a fatal outcome was a procedural complication. Increased operator experience as well as new technologic advances have the potential for decreasing the frequency with which these complications occur, although given the advanced age of the patients, the associated diseases and the large size of the equipment used, complications undoubtedly will remain.

Factors associated with complications. Not all complications were associated with marked increases in mortality. However, as would be expected, the more severe the complication, the higher the mortality rate; with myocardial perforation or ventricular tachycardia/fibrillation, the rate was 56% and 53%, respectively. The most important specific factors associated with increased complications were female gender, the presence of coronary artery disease and more severe functional class (New York Heart Association) at baseline. Other factors included the use of a double balloon technique and early experience in the study; as the study continued and as experience increased and equipment changed, the chance of complications decreased, mainly in relation to a decrease in vascular injury. Despite the statistically significant associations between these factors and the development of complications, the predictive value was low and the model predicted complications accurately in only 58% of the patients.

In most patients undergoing aortic valve dilation, there is only moderate improvement in aortic valve hemodynamics (3–6). During the follow-up period there is a substantial incidence of adverse cardiac events and a high incidence of restenosis (from 50% to 75%). Nevertheless, many patients, even those with restenosis continue to have symptomatic improvement. Because of this palliation in symptoms, the technique does offer benefits for select subsets of patients with severe aortic stenosis. Identifying which patients are associated with increased complications may improve patient selection and allow more accurate assessment of the risk/benefit ratio for this specific patient subset.

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